Arterial stiffness and ventricular stiffness: a couple of diseases or a coupling disease? A review from the cardiologist’s point of view

Francesco Antonini-Canterin1*, Scipione Carerj2, Vitantonio Di Bello3, Giovanni Di Salvo4, Salvatore La Carrubba5, Olga Vriz6, Daniela Pavan7, Alberto Balbarini3, and Gian Luigi Nicolosi1 on behalf of the Research Group of the Italian Society of Cardiovascular Echography (SIEC)

1Division of Cardiology, ARC, S. Maria degli Angeli Hospital, Via Montereale, 24, 33170 Pordenone, Italy; 2Institute of Cardiology, University of Messina, Messina, Italy; 3Cardiac and Thoracic Department, University of Pisa, Pisa, Italy; 4Department of Pediatric Cardiology, Second University of Naples, Monaldi Hospital, Naples, Italy; 5Department of Internal Medicine, Villa Sofia Hospital, Palermo, Italy; 6Division of Cardiology, San Daniele del Friuli Hospital, Udine, Italy; and 7Division of Cardiology, S.Vito al Tagliamento Hospital, S.Vito al Tagliamento, Italy

The assessment of arterial stiffness, a common feature of ageing, exacerbated by many common disorders such as hypertension, diabetes mellitus, or renal diseases, has become an attractive tool for identifying structural and functional abnormalities of the arteries in the preclinical stages of the atherosclerotic disease. Arterial stiffness has been recognized as an important pathophysiological determinant of systolic blood pressure and pulse pressure increases and therefore the cause of cardiovascular complications, demonstrating also an independent predictive value for cardiovascular events. Although there are many techniques and indices currently available, their large clinical application is limited by a lack of standardization, with important difficulties when one tries effectively to measure, quantify, and compare. Moreover, information on the ‘heart-vessel coupling disease’, in which combined stiffness of both heart and arteries interact to limit cardiovascular performance and its possible implications in different clinical conditions, is still not well known. We overviewed main methods and indices used to estimate arterial stiffness and aimed to provide an insight into the knowledge of the ventricular–arterial coupling from the cardiologist’s point of view.

KEYWORDS
Arterial stiffness; Ventricular stiffness; Ventricular–arterial coupling; Echo-tracking

In recent years, arterial stiffness and wave reflection phenomenon were identified as the most important pathophysiological determinants of systolic blood pressure (SBP) and pulse pressure (PP) increases and therefore the cause of cardiovascular (CV) complications and events.1 Arterial stiffness had also demonstrated an independent predictive value for CV events in patients with hypertension,2,3 diabetes mellitus,4 end-stage renal disease,5 in elderly subjects6 and in the general population.7 However, for many years, the concept of ‘arterial stiffness’ was used in the field of pathophysiological and epidemiological studies and not much regarded as being part of the clinical cardiologic arena. For the first time, the last (2007) European guidelines for the diagnosis and treatment of hypertension8 recommended the assessment of arterial stiffness, as an evidence of target organ damage.

The pathophysiological and clinical implications of the arterial stiffening should be considered together with the cardiac function, as it is known that the interaction between the heart and the arterial system, the ‘ventricular–arterial coupling’, could be a key determinant of CV performance. It has been observed that age-related vascular stiffening, which can seriously affect this coupling, is accompanied by changes in the left ventricular (LV) stiffness and diastolic compliance. Furthermore, this combined ventricular–arterial stiffening, referred to as ‘coupling disease’,10 appears to be common in patients with heart failure (HF) and preserved ejection fraction.11 Also, it has been shown that the accurate assessment of the haemodynamic severity of aortic stenosis has to consider the global LV afterload that include both the degree of the valvular obstruction and the arterial system properties.12,13
Thus, the concept of 'ventricular–arterial coupling' or even 'ventriculo–valvulo–arterial interaction' is becoming an issue of increasing interest with relevant clinical implication.

This article reviews some of the indices and methods used to estimate arterial stiffness, underlying the strengths and weaknesses of each one. Also, it aims to discuss the concept of ventricular–arterial interaction and its possible implications in different clinical conditions. It is a review realized from the cardiologist's point of view, emphasizing the role of ultrasound and echo-tracking systems, since these techniques allow an easy evaluation of both heart and vessels during the same examination.

Characteristics of the arterial tree and their clinical implications

The elastic properties of arteries vary along the arterial tree, with more elastic proximal arteries and stiffer distal arteries. The velocity of propagation of the pulse wave increases with decreased arterial distensibility. Moreover, wave reflections, which amplify the pressure wave, are generated at the level of peripheral arterial bifurcations and smaller muscular arteries. The net result is a progressive increase in both SBP and PP from the heart to the periphery, called 'amplification phenomenon'. Therefore, the brachial blood pressure (BP) is not always a reliable measure of the central aortic pressure. In young subjects, especially, the brachial BP overestimates central pressure, whereas in older subjects there is a stiffening of central arteries and consequently a lower amplification of PP from central to peripheral blood vessels. Central aortic pressure represents better the load imposed on the coronary and cerebral arteries and thereby should be better related to vascular damage and prognosis. In the Strong Heart Study, central PP was more strongly related to carotid artery hypertrophy, extent of atherosclerosis, and incidence of CV events than the brachial PP. On the contrary, data from the Second Australian National Blood Pressure Study, in older hypertensive female patients, showed no benefit of central arterial waveform analysis (central SBP, central PP, augmentation index, and systemic arterial compliance) over brachial cuff BP in predicting CV events, possibly because of the lack of amplification of PP from the heart to the periphery at this age.

Arterial stiffness: indices and methods of assessment

Arterial stiffness can be assessed as local, regional, and systemic stiffness. Although systemic arterial stiffness may only be estimated, local and regional stiffness can also be measured. Direct measurement of arterial stiffness implies the measurements of change in arterial diameter and pressure at the same site. This could be performed invasively or non-invasively. Diameter changes can be determined accurately, especially with high-definition echo-tracking systems, but the estimation of the pressure changes at the same site may be difficult because of the amplification of the PP and inaccuracy of all cuff sphygmomanometer systems. Indices of local stiffness are: distensibility (the relative change in diameter with pressure), compliance (the absolute change in diameter or area with pressure), Peterson's elastic modulus (pressure change required for theoretic 100% increase in diameter), Young's elastic modulus (pressure change per square centimetre for theoretic 100% extension). A non-dimensional index of local arterial stiffness frequently used is the stiffness index β [ratio of logarithm (systolic/diastolic pressures) to relative change in diameter] (Table 1).

![Figure 1](Figure 1) Examination of the common carotid artery with simultaneous display of waveforms derived from instantaneous changes in diameter using echo-tracking technique.
Pulse wave velocity

Pulse wave velocity (PWV) is accepted as the most simple, robust, and reproducible method to determine the regional arterial stiffness. There is a linear correlation between the speed of travel of pulse along an arterial segment and arterial stiffness. To calculate PWV, the distance between the two sites at which the wave is being recorded is divided by the time of travel of the wave from the first to the second site:

\[
PWV = \frac{\text{distance}}{\text{time}}
\]

It is usually measured using the foot-to-foot velocity method from various waveforms at different sites (pressure, distension, or Doppler waveforms) (Figure 2). The normal values of PWV increase from 4–5 m/s in the ascending aorta to 5–6 m/s in the abdominal aorta then 8–9 m/s in the iliac and femoral arteries. Carotid-femoral PWV is considered as the ‘gold-standard’ measurement of arterial stiffness and has been largely used in epidemiological studies demonstrating a strong independent predictive value for CV events. The major limitation of this index derives from the inaccuracy of distance measurement, which could theoretically be overcome using methods based on Doppler probes or echo-tracking systems with measurements made at the root of the left subclavian artery (suprasternal notch) and near the bifurcation of the abdominal aorta (umbilical level). Also, it could be difficult to record the femoral pressure waveform in patients with obesity, diabetes, and peripheral artery disease. In addition, sometimes the thoraco-abdominal aorta is quite straight, but often it is very curvilinear, so the external measure could be inaccurate.

Echo-tracking systems allow the assessment of local arterial stiffness deriving the pressure–diameter curve of the artery (the measurements of stroke changes in diameter and local PP should be determined simultaneously) and calculating the local PWV from the time delay between the two adjacent distension waveforms. With some echo-tracking systems (Prosound Alfa 10; Aloka, Tokio, Japan), it is also possible to measure local PWV from the time delay between the two adjacent distension waveforms. With some echo-tracking systems (Prosound Alfa 10; Aloka, Tokio, Japan), it is also possible to measure local PWV from the time delay between the two adjacent distension waveforms.

Table 1  Indices of local arterial stiffness (modified after O’Rourke et al.\(^{19}\))

<table>
<thead>
<tr>
<th>Index</th>
<th>Definition</th>
<th>Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial distensibility</td>
<td>Relative diameter (or area) change for a pressure increment</td>
<td>((\Delta D/\Delta P \times D) \text{ (mmHg}^{-1}) (\Delta D/\Delta P \text{ (cm/mmHg)} ) or (\text{cm}^2/\text{mmHg})</td>
</tr>
<tr>
<td>Arterial compliance</td>
<td>Absolute diameter (or area) change for a given pressure step at fixed vessel</td>
<td>((\Delta D \times D/\Delta D) \text{ (mmHg)})</td>
</tr>
<tr>
<td>Elastic modulus</td>
<td>The pressure step required for (theoretical) 100% stretch from resting</td>
<td>((\Delta P \times D/\Delta D) \text{ (mmHg)})</td>
</tr>
<tr>
<td>Young’s modulus</td>
<td>diameter at fixed vessel length</td>
<td>((\Delta D \times D/\Delta D \times h) \text{ (mmHg/cm)})</td>
</tr>
<tr>
<td>Stiffness index (\beta)</td>
<td>Ratio of logarithm (systolic/diastolic pressures) to relative change in</td>
<td>(\ln(P_s/P_d)/[[D_s - D_d]/D_d]] \text{ (non-dimensional)} )</td>
</tr>
</tbody>
</table>

Figure 2  The foot-to-foot velocity method for the measurement of two points PWV.

Regional aortic stiffness and carotid stiffness, although providing similar information on the effect of ageing on elastic arteries stiffening in normal subjects, are not interchangeable predictors in high-risk patients, such as hypertensive or diabetic subjects. It has to be considered that in this type of patients, the aorta stiffened more than the carotid artery, with age and other CV risk factors.

Central pulse wave analysis

The arterial pressure waveform is a composite of the forward wave created by LV contraction and a reflected wave generated in the periphery, returning towards the heart. The central pulse wave should be analysed through three major parameters: central PP, central SBP, and augmentation index (Alx).\(^{14}\)

In elastic vessels, PWV is low and the reflected wave can reach the ascending aorta after the aortic valve has closed, in diastole, increasing central diastolic pressure (DBP) and coronary perfusion, central SBP remaining unchanged. Reduced compliance of the large arteries increases the PWV and backwards wave from the periphery returns early to the ascending aorta, during systole, increasing central SBP (phenomenon quantified through the Alx)
Arterial stiffness and ventricular stiffness

and decreasing central DBP and coronary perfusion pressure. Alx (Figure 3) is calculated as the ratio between the augmentation pressure (AP) and PP and is expressed in percentage:

\[
\text{Alx} = \frac{\text{AP}}{\text{PP}}
\]

where AP is the difference between maximal pressure and pressure at the first peak (shoulder) on pulse waveform and PP is the difference between SBP and DBP.

Thus, Alx is a complex composite measurement, derived from many important dynamic variables. It is influenced by PWV, the reflectance point, and LV ejection characteristics, especially with respect to change in heart rate and ventricular contractility. It has been shown that Alx is also influenced by BP, age, gender, body height, and especially heart rate.

Central Alx and PP proved to be independent predictors of mortality in end-stage renal disease, in patients undergoing percutaneous coronary intervention and in hypertensive patients.

On the other hand, a recent study demonstrated that in patients with systolic hypertension the pathogenesis of increased PP seems to be due to increased wall stiffness and reduced aortic diameter rather than to the premature wave reflection.

Arterial compliance

Arterial compliance can be either directly measured (i.e. using an echo-tracking system) as an index of local arterial compliance or calculated as systemic or total arterial compliance (SAC), using the so-called ‘area method’

\[
\text{SAC} = \frac{A_d}{R (P_s - P_d)}
\]

where \(A_d\) is the area under the BP diastolic decay curve from end-systole to end-diastole, \(R\) the total peripheral resistance, \(P_s\) the end-systolic BP, and \(P_d\) the end-diastolic BP. Also, SAC can be estimated from the ratio of stroke volume to PP, but this method is considered to be a crude approximation. It is known that SAC decreases with age in both men and women. The SAC has also been correlated with disease status and common CV risk. It has been shown that the changes in the central and/or peripheral arteries can affect SAC in patients with hypertension, diabetes, and hyperlipidaemia. A very recent study issued that age and other irreversible risk factors (such as height and weight) are the major determinants of SAC and thus questioning its role as marker of arterial stiffness and guide to therapy. Furthermore, until now, except for one study, there is no strong evidence that SAC has independent predictive value for CV events.

Other indices of arterial stiffness

Characteristic impedance is another index that relates absolute arterial pressure at a site to absolute velocity of flow at the same site in the absence of wave reflections. Since the exclusion of the effects of wave reflection is difficult, when using non-invasive methods, another index was proposed to adjust for the logarithmic relationship between stiffness indices and pressure—the stiffness index \(\beta\):

\[
\beta = \frac{\ln(P_s/P_d)}{(D_s - D_d)/D_d}
\]

where \(P_s\) is the end-systolic BP, \(P_d\) the end-diastolic BP, \(D_s\) the end-systolic diameter and \(D_d\) the end-diastolic diameter. The stiffness index \(\beta\) is less affected by arterial pressure changes and could be more useful than other parameters, being easily determined using echo-tracking devices (Figure 4). Carotid stiffness index \(\beta\) has been recently evaluated in CV diseases, such as myocardial infarction, aortic stenosis, or various other clinical conditions (haemodialysis, hypothyroidism, or hyperthyroid Graves’ disease).

The concept of ventricular–arterial coupling

The ventricular–arterial coupling, meaning the interaction of the heart with the systemic vasculature, is a key determinant of CV performance, influencing both magnitude and efficiency of transfer of LV stroke work to the circulation. The capacity of the body to increase cardiac output, regulate systemic BP, and respond appropriately to elevations in heart rate and preloads depends on both the properties of the heart and the vessels into which the heart ejects blood. Normal physiological ventricular–arterial coupling matches these properties, so that maximal cardiac work, power, and chamber efficiency are achieved while maintaining BP and cardiac outputs within a physiological range. The ventricular–arterial coupling can be accurately quantified in the pressure–volume plane. Left ventricular performance can be characterized by the slope of the end-systolic pressure–volume relation—end-systolic elastance (\(E_{es}\)). \(E_{es}\) is a measure of end-systolic LV stiffness and can be determined invasively or can be estimated non-invasively by the formula:

\[
E_{es} = \frac{P_d - (E_{Nd(est)} \times P_s \times 0.9)}{E_{Nd(est)} \times SV}
\]

where \(P_s\) and \(P_d\) are systolic and diastolic arm-cuff pressures, \(E_{Nd(est)}\) is an estimated normalized ventricular elastance at arterial end-diastole (or at the onset of ejection) and \(SV\) is the echocardiography stroke volume.

The arterial system can be similarly assessed using the slope of the arterial \(P_{es}\)–stroke volume relation—effective arterial elastance (\(E_a\)). \(E_a\) is a measure of impedance (being influenced by static and pulsatile afterload and by
heart rate) \(^{41}\) and is calculated as: \(^{42}\)

\[ E_a = \frac{P_{es}}{SV} \]

where \(P_{es}\) is the end-systolic pressure, measured or estimated non-invasively as \(P_s \times 0.9\), and \(SV\) is stroke volume.

In this manner, both LV and arterial system could be considered elastic chambers with known volume elastances, with the \(E_a/E_{es}\) ratio serving as a reliable index of ventricular–arterial coupling. Under normal conditions, the LV and arterial system are nearly optimal coupled, operating at an \(E_a/E_{es}\) ratio close to 1 (0.3–1.3) \(^{41}\) resulting in maximal stroke work and cardiac metabolic efficiency. In contrast, in HF due to LV systolic dysfunction, ventricular–arterial coupling is suboptimal, as \(E_{es}\) is decreased (pump dysfunction) while \(E_a\) is generally increased (increased impedance and decreased compliance). Furthermore, there is some evidence that ventricular–arterial coupling defects occur prior to significant pump dysfunction. \(^{39}\)

The LV systolic and diastolic stiffness increases in tandem with arterial stiffening in various conditions. Such combined stiffening alters heart–arterial system interactions at rest and under stress by exertion, salt loading, and abrupt changes in heart function. So, combined ventricular–arterial stiffening impacts on CV reserve, BP lability, diastolic function, coronary and peripheral flow regulation, and endothelial function. In this context, the concept of stiff heart artery coupling disease was proposed. \(^{10}\) The most important condition in which arterial stiffening is accompanied by increasing LV stiffness is age. \(^{9}\) In the elderly, the heart appears to develop an increase in both diastolic and systolic LV stiffness, with or without hypertrophy. The higher \(E_{es}\), expected from arterial stiffening, is associated with an increase in \(E_{es}\) (reflecting chamber geometry and structural alterations in the myocardium with age). A rise in both ventricular and arterial elastances means that the \(E_a/E_{es}\) ratio is essentially preserved despite age-related changes in each system. Although this matched increase of arterial and cardiac stiffness can maintain ventricular–arterial coupling within a normal range, it impacts the haemodynamic stability and cardiac reserve. As consequence, the systemic circulatory compliance is reduced generating larger changes in pressure for any given change in ejected volume, resulting in a greater BP lability. In addition, there is also limitation of the reserve mechanisms. During exercise, \(E_a\) typically rises because of the increased heart rate and arterial pulsatility and \(E_{es}\) also rises because of the contractile increase. When basal \(E_a\) and \(E_{es}\) are already elevated, there is less reserve and any increase in \(E_a\) will only exacerbate systolic hypertension. \(^{38}\) Furthermore, altered coupling influences myocardial perfusion by elevating the proportion of coronary flow during systole (up to 50%). Another effect of the change in coronary flow pattern due to ventricular–arterial stiffening is worsening the impact of regional coronary ischaemia when a decline in ventricular systolic performance and systolic pressure occurs. \(^{38}\)

The presence of ventricular–arterial stiffening induces higher BP sensitivity to circulating volume and diuretics, thus rendering more difficult the treatment of HF, especially of HF with a preserved cardiac ejection fraction. The role of ventricular and arterial stiffness in the pathophysiology of HF with preserved ejection fraction is beyond the association with age and hypertension, \(^{11}\) an increased ventricular–arterial stiffness worsening diastolic function, augmenting BP lability, and elevating cardiac metabolic demand under stress. Therefore, an increased systolic ventricular–arterial stiffness is one of the pathological mechanisms in HF with normal ejection fraction, together with LV diastolic dysfunction (impaired relaxation and increased passive diastolic stiffness) and cardiac volume overload. A recent large, population-based study \(^{43}\) showed that, although patients with HF with normal ejection fraction display arterial and LV systolic stiffening, the presence and progression of diastolic dysfunction could be more important, as confirmed by another study performed invasively in patients with HF and normal ejection fraction. \(^{44}\)

Figure 4  Echo-tracking assessment of carotid stiffness parameters (\(\beta\) index, augmentation index, arterial compliance, and PWV).
An important aspect of ventricular–arterial coupling is the great impact of arterial stiffness on LV diastolic function in different populations: in patients with CV risk factors, hypertension, diabetes, ESRD, obstructive sleep apnea, and in a population-based cohort study. Arterial stiffness was assessed using different indices: PWV, arterial compliance, carotid stiffness (Peterson’s elastic modulus, Young’s elastic modulus, and distensibility coefficient), central PP, aortic strain, and distensibility. Attempts have been made to identify the most accurate arterial stiffness index in detecting preclinical LV diastolic dysfunction: aortic PP, brachial PP and PWV seem superior to AP, and PWV appears to be superior to central and brachial PP in older subjects. A correlation between arterial stiffness and left atrial size, an index of ventricular diastolic function, was described; being emphasized as a new possible pathophysiological link between arterial stiffness and stroke, as the left atrial dilatation is a risk factor for atrial fibrillation.

Arterial stiffness seems to impact also the regional ventricular function in patients with HF and normal ejection fraction: LV longitudinal function and LV circumferential strain.

Another rough measure of ventricular–arterial coupling is the ratio between LV force, estimated as SBP divided by LV systolic volume index, and $E_a$, which proved to be influenced by pharmacological stress in normal subjects and patients with coronary artery disease or dilated cardiomyopathy.

Given the implication of ventricular–vascular coupling in such pathological conditions, its assessment becomes of clinical importance. The echo-tracking systems allow us to obtain information about both ventricular and arterial functions and their coupling during the same examination.

Wave intensity

Wave intensity (WI) is another hemodynamic index which gives an image of ventricular–arterial coupling. Its advantages are the possibility of being measured non-invasively with echo-tracking systems and the sensitivity to changes in the working conditions of the heart interacting with arterial system and conditions of the peripheral circulation. It also provides information about the forward and the backward traveling waves, can be determined at any site of the circulatory system, and was initially defined as the product of $\Delta P$ and $\Delta U$, where $\Delta P$ and $\Delta U$ are the changes in BP and blood velocity during constant short-time intervals. The original WI depends on the sampling interval, $\Delta t$. The time-normalized WI is the product of derivatives of $P$ and $U$ with respect to time:

$$\text{WI} = \left( \frac{dP}{dt} \right) \times \left( \frac{dU}{dt} \right)$$

If WI is greater than zero, the changes in pressure and velocity caused by the forward travelling wave from the ventricle to the periphery are greater than those caused by the backward travelling wave.

In normal subjects, carotid arterial WI has two positive peaks (Figure 5). The first peak $W_1$ appears during early systole and its magnitude increases with cardiac contractility and correlates with the maximum rate of LV pressure rise. The second peak $W_2$ occurs towards the end of ejection, relates to the ability of the LV to actively stop aortic blood flow, and correlates with the time constant of LV relaxation. Between these two positive peaks, a negative area signifies reflections from the cerebral circulation. WI could be a useful parameter for the evaluation of LV systolic and early diastolic performance simultaneously, as its first peak reflects the LV contractile function, while the amplitude of the second peak is determined by LV behaviour during the period from late systole to isovolumic relaxation. WI assessment was found to predict hemodynamic deterioration in patients with end-stage dilated cardiomyopathy referred for transplantation.

![Figure 5](Automated assessment of carotid arterial wave intensity.)
Predictive value of arterial stiffness

An important body of evidence links increased PWV, elevated PP, and premature/increased arterial wave reflections with a higher risk of CV morbidity and mortality. Aortic stiffness has independent predictive value for all-cause and CV mortalities, fatal and non-fatal coronary events, and fatal stroke in hypertensive,2,4 diabetic,4 or renal5 patients, in elderly6 or healthy subjects61 and in the general population.7 Data concerning the independent predictive value of carotid stiffness, central Aix, and PP are scarce, as mentioned above. An increased PP is associated with the development of LV dysfunction and clinical HF in the elderly and in hypertensives.62

The independent predictive value of aortic stiffness has also been demonstrated after adjustment to classical CV risk factors.14 In this context, it is important to understand the prevalence and correlates of abnormally high aortic stiffness. Recent data63 from the Framingham Heart Study show that the prevalence of abnormal aortic stiffness increases steeply with advancing age in the community, especially in the presence of obesity and diabetes. In patients with asymptomatic LV dysfunction and systolic HF, there is a positive correlation between the elevated PP and an adverse outcome, a low PP being an independent predictor of mortality. An explanation for these findings could be the ventricular–arterial interaction. Because of ventricular–vascular coupling, central PP, SBP augmentation, and aortic PWV are altered in cardiomyopathy patients, especially in those with very low ejection fraction.62

Conclusion

Although arterial stiffness and wave reflection provide useful prognostic information concerning the CV events in different populations, the clinical value of arterial stiffness and wave reflection attenuation for the reduction in CV events under treatment remains largely to be demonstrated. A major issue would be to determine whether a reduction in PWV or wave reflection is associated with a concomitant reduction in CV events, independently of the normalization of classical risk factors. This is likely because arterial stiffness decrease reflects the true reduction of arterial wall damage, whereas the reduction in BP, glycaemia, and lipids may not.64 In this context, the measurement of arterial stiffness, wave reflection, and ventricular–arterial stiffness become of essential clinical interest. The implementation of ultrasound systems, such as echotracking devices embedded in echocardiographic machines, can provide a precise, non-invasive determination of arterial stiffness, and an assessment of ventricular–arterial interactions, determining a true impact in the clinical area of cardiologists.

Conflict of interest: none declared.

References


F. Antonini-Canterin et al.
Arterial stiffness and ventricular stiffness


